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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,317	06/15/2006	Nils-Olof Johansson	1003301-000275	3220

21839 7590 04/02/2009

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EXAMINER	
SCHLIENTZ, LEAH H	

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
04/02/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/583,317	JOHANSSON, NILS-OLOF	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 4-11, 13-18, 21, 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Pettersson *et al.* (WO 98/11922).

Petterson discloses the use of a physiologically tolerable manganese compound or a salt thereof, in combination with a second contrast agent, preferably one which is retained in the gut and exhibits a negative contrast effect, in the method of an orally or rectally administratable MRI contrast medium composition for use in a functional method of imaging of the gastrointestinal tract of a human or non-human animal body (abstract). The compositions further include an uptake promoter, examples of acids which have been found to be particularly effective include amino acids, e.g. alanine, aspartic acid, arginine, etc. The molar ratio of manganese to uptake promoter is from 1:0.2 to 1:50, e.g. preferably 1:1 to 1:6. Alternatively, the molar ratio of manganese to uptake promoter may be in the range of from 1:1.5 to 1:5 (page 9, second and third paragraphs). Methods include enhanced imaging of the abdomen as a whole, in particular the liver (page 11, third paragraph). The dosage of manganese is from 5 to 500 μg/kg bodyweight, preferably from 5 to 150 μg/kg, more preferably from 10 to 100

μg/kg, while the dosage of the uptake promoter may be in the range of 5 μmol to 1 μmol/kg bodyweight (page 13, first paragraph). See also claims 17-19.

Claims 2, 4-11, 13-19, 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomsen (US 6,015,545).

Thomsen discloses a composition for use as a contrast medium being particularly suitable for imaging of the stomach, liver, bile duct and gall bladder, said compositions comprising as an active ingredient a physiologically acceptable manganese compound and an uptake promoter, wherein said uptake promoter comprises a physiologically acceptable reducing compound comprising a physiologically acceptable amino acid and/or vitamin D (abstract). The manganese compound includes a salt, chelate or complex (column 2, lines 64+). Amino acids which are effective uptake promoters include alanine, aspartic acid, etc. (column 3, lines 13-21). MR images of the liver of rats after administering the contrast medium composition orally (column 3, lines 28-29). The preferred molar ratio of manganese to uptake promoter is from 1:0.2 to 1:50, preferably 1:1 to 1:20, more preferably 1:3 to 1:6 (column 4, lines 1-2). It is possible to formulate the contrast medium immediately or shortly prior to administration by mixing the uptake promoter with the manganese species, including kits comprising a in a first container a physiologically acceptable manganese compound, and in a second container an amino acid compound and/or vitamin D (column 5, lines 1-8). The dosage of manganese will be in the range from 5 to 500 μg/kg bodyweight, preferably from 5 to 150 μg/kg, more preferably from 10 to 100

μg/kg, while the dosage of the uptake promoter may be in the range of 5 μmol to 1 μmol/kg bodyweight (column 5, lines 32-42).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 2-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pettersson *et al.* (WO 98/11922) and Thomsen (US 6,015,545).

Pettersson and Thomsen disclose compositions as orally administratable MRI contrast agents, as set forth above. Petterson and Thomsen teach molar ratio of manganese to amino acid uptake promoters in the range from 1:0.2 to 1:50, e.g. preferably 1:1 to 1:6; or in the range of from 1:1.5 to 1:5 (i.e, such ranges correspond to 5:1 to 0.02:1).

While Petterson and Thomsen do not specifically recite that the molar ratio of manganese to amino acid in the formulation is from 2:1 to 3:1, it would have been obvious to one of ordinary skill in the art to optimize the ranges of manganese to amino acid within the broader ranges disclosed by Petterson and/or Thomsen. For example, Petterson and/or Thomsen clearly envisaged manganese in excess to amino acid (i.e. 5:1), manganese in equivalent amount to amino acid (i.e. 1:1), or manganese in various lower amounts than amino acid. The claims differ from the reference only by reciting various concentrations of the active ingredient(s). However, the preparation of pharmaceutical compositions having various amounts of the active agent was within the level of skill of one having ordinary skill in the art at the time of the invention. With these things in mind a skilled artisan would have been motivated to combine the teachings of Pettersson and Thompson in order to provide an orally administratable contrast agent comprising manganese and amino acid within the claimed molar ratio with a reasonable expectation of success in achieving a stable composition providing MR contrast of liver. See also *In re Peterson*, 315 F3d at 1330, 65 USPQd at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.")

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS